INTERNATIONAL SEARCH REPORT

| Patent document cited in search report | | Publication date | | Patent family member(s) | Publication date |
|---|----|--------------------------------------|------|----------------------------|------------------|
| US 2003087316 | A1 | 08-05-2003 | NONE | | —- L. |
| JP 2003252792 | T | , | NONE | | |
| - | | . بروران به مه مهمان بیب بها ۱۳۰۳ شا | | | |
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INTERNATIONAL SEARCH REPORT

International Application No EP2005/000607

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C1201/37 G01N33/573

G01N33/68

A61K38/00

A61K39/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Form PCT/ISA/210 (second sheet) (January 2004)

Minimum documentation searched (classification system followed by classification symbols) IPC $\frac{7}{2}$ C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to ctaim No. |
|------------|---|-----------------------|
| X | US 2003/087316 A1 (HUGLI TONY E ET AL) 8 May 2003 (2003-05-08) the whole document | 1-26 |
| X | JP 2003 252792 T (INST OF PHYSICAL & CHEMICAL RES; GIFU UNIV) 10 September 2003 (2003-09-10) '0009!;claims 1-4 | 1–26 |
| X | CIECHANOWICZ ANDRZEJ ET AL: "Plasma prekallikrein levels in patients with hepatocellular carcinoma and liver cirrhosis: A pilot study" ANNALS OF CLINICAL BIOCHEMISTRY, vol. 30, no. 5, 1993, pages 445-448, XP009051085 ISSN: 0004-5632 the whole document | 1-26 |

| Further documents are listed in the continuation of box C. | Patent family members are listed in annex. | | |
|---|--|--|--|
| Special categories of cited documents: 'A' document defining the general state of the art which is not considered to be of particular relevance 'E' earlier document but published on or after the International filing date 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O' document referring to an oral disclosure, use, exhibition or other means 'P' document published prior to the international filing date but later than the priority date claimed | "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family | | |
| Date of the actual completion of the international search | Date of mailing of the international search report | | |
| 28 July 2005 | 1 5. 09. 2005 | | |
| Name and mailing activess of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016 | Authorized officer Jacques, P | | |

10/588234

IAP11 Rec'd PCT/PTO 03 AUG 2006

| C.(Continua | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | International Application No PEP2005/000607 |
|-------------|---|---|
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Policipal to Advanta |
| | Face general section of the section | Relevant to claim No. |
| X | AGNHOLT J ET AL: "PLASMA PREKALLIKREIN AS A PROGNOSTIC INDICATOR IN CHRONIC LIVER INSUFFICIENCY" SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY, vol. 25, no. 1, 1990, pages 40-44, XP009051084 ISSN: 0036-5521 the whole document | 1-26 |
| X | DATABASE MEDLINE 'Online! US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; November 1995 (1995-11), CIECHANOWICZ A ET AL: "'Plasma prekallikrein in chronic liver diseases!" XP002337464 Database accession no. NLM8833936 abstract & POLSKIE ARCHIWUM MEDYCYNY WEWNETRZNEJ. NOV 1995, vol. 94, no. 5, November 1995 (1995-11), pages 395-401, ISSN: 0032-3772 | 1-26 |
| x | NAGAOKA MARCIA R ET AL: "Hepatic clearance of tissue-type plasminogen activator and plasma kallikrein in experimental liver fibrosis." LIVER INTERNATIONAL, vol. 23, no. 6, December 2003 (2003-12), pages 476-483, XP002337288 ISSN: 1478-3223 the whole document | 1-26 |
| X | MERLO C ET AL: "Elevated levels of plasma prekallikrein, high molecular weight kininogen and factor XI in coronary heart disease" ATHEROSCLEROSIS, AMSTERDAM, NL, vol. 161, 2002, pages 261-267, XP002316792 ISSN: 0021-9150 the whole document | 1-26 |
| | | |
| i | | 1 |

INTERNATIONAL SEARCH REPORT



| Box II | Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet) |
|-----------|--|
| This Inte | ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. X | Claims Nos.: 26 because they relate to subject matter not required to be searched by this Authority, namely: |
| | Although claim 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. |
| 2. | Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| | |
| 3 | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box III | Observations where unity of invention is lacking (Continuation of item 3 of first sheet) |
| This inte | emational Searching Authority found multiple Inventions in this international application, as follows: |
| | see additional sheet |
| 1. | As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims. |
| 2. | As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. | As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| 4. X | No required additional search fees were timely paid by the applicant. Consequently, this international Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-26 (all partially) |
| Remark | on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees. |
| L | |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-26 (all partially)

Methods of screening for therapeutic agents useful in the treatment of liver cirrhosis. A method for diagnosing liver cirrhosis. Pharmaceutical compositions for the treatment of liver cirrhosis. Use of regulators of a KLKB1 for the preparation of a pharmaceutical composition for the treatment of liver cirrhosis. A method for the preparation of a pharmaceutical composition useful for the treatment of liver cirrhosis. Use of a regulator of KLKB1 for the regulation of KLKB1 activity in a mammal having liver cirrhosis (see p. 44 (gastrointestinal and liver diseases), p.51 (inflammatory diseases), p. 53 (metabolic diseases)).

2. claims: 1-26 (all partially)

Same subject-matters as invention 1 but relating to liver tumor (see page 50).

3. claims: 1-26 (all partially)

Same subject-matters as invention 1 but relating to Alzheimer disease (see page 41).